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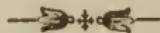




AN  
INQUIRY  
INTO THE  
MODUS OPERANDI  
OF THAT CLASS OF MEDICINES  
CALLED  
SEDATIVES:  
SUBMITTED, AS AN  
INAUGURAL DISSERTATION,  
TO THE  
EXAMINATION  
OF THE  
REV. JOHN EWING, S. T. P. PROVOST;  
THE  
TRUSTEES & MEDICAL FACULTY,  
OF THE  
UNIVERSITY OF PENNSYLVANIA,  
On the thirty-first of May 1800,  
FOR THE DEGREE OF  
DOCTOR OF MEDICINE.

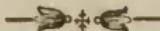
11370  
—♦♦—  
BY ROBERT BERKELEY, OF VIRGINIA,

MEMBER OF THE PHILADELPHIA MEDICAL AND CHEMICAL SOCIETIES.



“ Nendum sermonum stet honos, et gratia vivax.  
“ Multa renascentur, quæ jam cecidere; cadent que,  
“ Quæ nunc sunt in honore —————, si volet usus;  
“ Quem penes arbitrium est, et jus, et norma” Scribendi

HORACE ARS POETIC.



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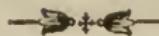
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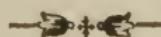
TO  
CARTER BERKELEY, M. D.  
OF VIRGINIA,  
THIS  
*E S S A Y*  
IS INSCRIBED,  
BY  
HIS SINCERE FRIEND,  
AFFECTIONATE BROTHER,  
AND GRATEFUL PUPIL,  
THE AUTHOR.

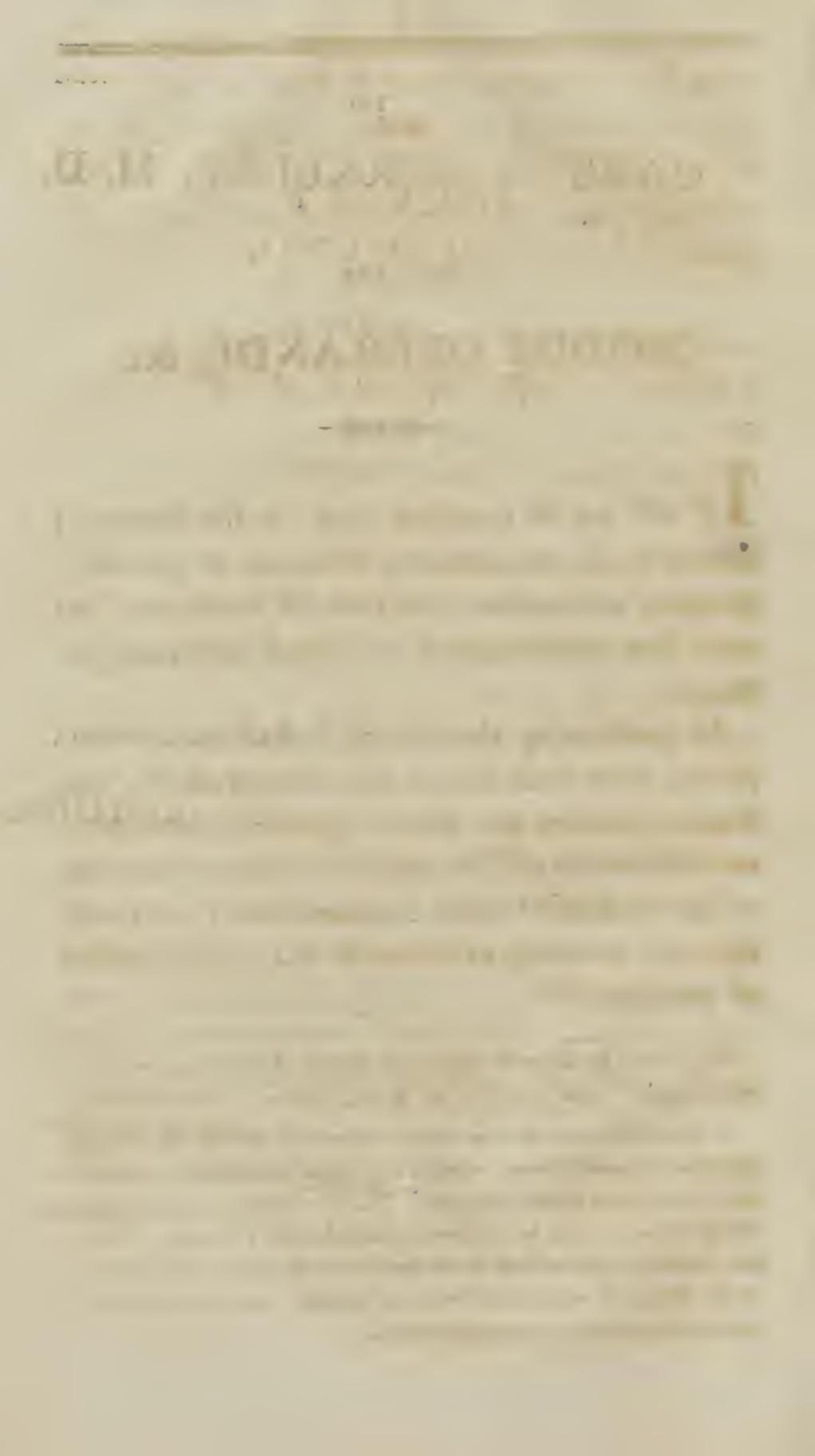
May 31<sup>st</sup>, 1800.



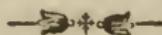
“ Ut Pictura \_\_\_\_\_, erit quæ, si propius stes,  
“ Te capiat magis; et quædam, si longius abstes:  
“ \_\_\_\_\_; volet hæc sub luce videri,  
“ Judicis argutum quæ non formidat acumen;  
“ Hæc placuit semel; hæc decies repetita placebit.  
At “ *Hæc amat obscurum.*” \_\_\_\_\_

HORACE ARS POETICÆ.





AN  
INQUIRY  
INTO THE  
MODUS OPERANDI, &c.



IT will not be expected, that, in this Inquiry, I should decide the question; What are all the effects properly ascribed to this class of medicines? but only *how* those imputed or allowed effects are produced.

In prosecuting the subject, I shall endeavour to prove, from these known and allowed effects, that these medicines are, strictly speaking, stimulants; or disprove the positive and direct sedative operation of any medicine \* upon the human body; of course then the propriety of having such a class or division of medicines.†

\* “ It may be observed, that all the articles of the *materia medica* act as stimulants.” *MS. note from Dr. Barton’s lectures on materia medica.*

† Under the term *Medicine*, we do not mean to include cold, insensible depletion, or even dilution; when it is intended to add these, we shall use more definite and explicit language. The two former, if without concomitant irritation, may be sedatives, as they abstract a stimulus. The primary effect of dilution must be ascribed to the change it produces in some of the stimuli to which our bodies are exposed: we say nothing of its mechanical operation, or its temperature.

We say, a direct sedative operation, and upon the human body in general, not any particular system or division of that body. "These are the medicines which directly and without evacuation diminish the powers and motions of the human body."\*

No medicine that increases action or excitement in one part, while it abstracts it from, or diminishes it in another, (though that part be more within the reach and under the observation of our senses) can properly be called a sedative.

Stripes, fractures and bruises from falls, the hot and cold bath, have been known to suspend and even cure mania, by creating a new action in the parts injured, or upon the surface of the body, and thus abstracting morbid action from, or diminishing it in, the brain.

We are told digitalis diminishes the frequency of the pulse; but it is a diuretic: Dr. Darwin's tincture is a violent emetic. By its stimulus then, it either increases the force of the pulse, thus diminishing that frequency depending on debility; or by abstracting sensibility, irritability, or excitability, from the blood-vessels, consequently action, it consumes it in the stomach.†

When an emetic is given, it induces nausea, & slight rigors take place in various parts, the pulse generally becomes weak, quick and irregular, the

\* Cullen's *materia medica*.

† Or by creating a new action.

face and lips grow pale, the eyes become dull, the countenance dejected, and a general debility seems to pervade the whole body. Dr. Darwin observes, "there seem to be some things, as a solution of a few grains of arsenic taken into the stomach, which can stimulate that organ immediately into such violent action, as to be instantly succeeded by paraly sis, and even death, and this without our perceiving its mode of operation."\*

In the febris controversa, of Dr. Sydenham, or the intestinal state of fever, of Dr. Rush, under the forms of diarrhea, dysentery, or cholic, blisters are often found useful.

Dr. Hartley gave a dog nux vomica, afterwards whipped him severely, which prevented the medicine from operating : here, by exciting morbid action on the surface, it is lessened in the primæ viæ.

Pneumonicula, or pulmonary consumption, sometimes alternates with rheumatism, diarrhea and mania.

Mr. Hunter is of opinion, that "mercury operates upon the principle of destroying the diseased action of the living parts, counteracting the venereal poison, by producing another action of a different kind."†

"It is well known that chancres generally stop spreading, or heal up, when the patient catches a fever," depending on this, "that the actions

" of the body are totally changed by the superior irritation that occasions the fever."\* Here we see one diseased action removed for the time, or altogether, by another action, or stimulating operation, from a new disease, or remedy applied.

Neutral salts are termed refrigerents, (the second head of Dr. Cullen's sedatives); Mr. Moore, a late writer on *materia medica*, remarks, " these substances, when acting as tonics, diuretics or purgatives, derive their power from a stimulating quality; yet the stimulus in all these substances is local, only exciting the parts with which they are in immediate contact, and their action upon the body in general is cooling and sedative."†

Dr. Darwin observes, " small doses of emetic tartar and ipecacuanha, and large doses of nitre, by producing nausea, debilitate and lessen the energy of the circulation, and are thus found useful in inflammatory diseases."‡

We find then, that the impression of a new disease, and the action of stimulants are attended with the phenomena, and the latter may, upon partial observation, be considered as entitled to the appellation of direct sedatives: we see the absurdity and impossibility of deciding, with any accuracy, upon the operation, or mode of operation, of medicines, when we attend to their effects upon a disease only, or the immediate seat of disease; upon one or several

\* *Moore's Materia Medica.*

† *Mat. Med.*

‡ *Zoonomia.*

divisions of the body alone, though that or these be the most important, whether we consider their extent or consequence to life.

Happy æra in medicine will that be indeed, when on the most extensive, as well as minute, investigation, the penetrating eye of genius, united with every talent for observation, and every incentive to application, shall explore this Dedalean intricacy, and explain the operation, or mode of operation of medicines upon the human body. It is its life; it is its possessing motion, sensation and thought, that causes the difficulty. Chemistry indeed, when confined to matter, more simply, as such, gives much satisfactory information; but it is inadequate to the task, while that matter possesses animal and even vegetable life. Does chemical analysis teach us, that muscular fibre will contract, a nerve convey impression and sensation, a vessel carry, return, absorb, secrete, or excrete fluids? Nay, does it teach that mercury will salivate, ipecacuanha vomit, jalap purge, or opium induce sleep?

Not venturing to trace out an untrodden path for myself, the principles, and in many instances the language, in which I have been educated, will be the limits prescribed to these observations; saying nothing in regard to my own credulity or scepticism about them.

Doctor Cullen, to prove the sedative effects of medicines, assumes the hypothesis, "of a subtile

“ elastic fluid existing in the medullary substance of  
 “ the brain and nerves ; upon the motions of which  
 “ all sense and vital motion depend ;”\* which mobility  
 he supposes may not only be diminished, but even  
 destroyed directly by these medicines. Not contented  
 with this he imagines another ; “ that fluid which  
 “ is under peculiar modifications in the moving fi-  
 “ bres, and gives them what we name the inherent  
 “ power.”† On this he thinks stimulants act ; and  
 to compleat the ingenious theory, remarks, “ the  
 “ apparent stimulating effects” (which he is obliged  
 to allow these medicines possess in a degree) “ are  
 “ not to be ascribed to a direct stimulating operation  
 “ or power which this class possesses,” but to (a  
 third hypothesis) “ an indirect operation, a law of  
 “ the animal œconomy defined to be a resistance  
 “ and consequent activity, which the animal œco-  
 “ nomy enjoys suited to oppose every application  
 “ that has a tendency to hurt it.”‡ I am of opinion  
 we had much better lay aside this *law* for the pre-  
 sent, which, like Bishop Berkeley’s matter, has been  
 said, *only to be perceived by the ideas* ; and not hav-  
 ing any incontrovertible proof of a *vis insita*, in-  
 herent power, or life in the solids independent of  
 nerves, we must not reason from the second sup-  
 position neither.

This vital principle, this spirit of animation, nerv-  
 ous power, mobility, irritability, sensibility, stimu-  
 lability, excitability, or whatever we please to term

\* Treatise on Mat. Med.

† Ibid.

‡ Ibid.

II

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it, be it a quality or substance, has been generally thought to be seated in the brain and nerves. It is said to be excited, impressed or acted upon through the mind, organs of sense and other parts of the body. The substances that compose our *materia medica*, act upon the same principles and in the same manner, making allowance for the difference of circumstances attending each. Therefore they have been all called stimulants of late; and properly divided into more general or diffusible, and more local or fixed.

Here I would direct the attention to Dr. Cullen's general distinction between stimulants and sedatives: in his comparative definition of the two, he says, "there are substances, which, applied to the nerves, have a power of increasing or diminishing the mobility of the fluid in them. The former are named stimulants, the latter sedatives." §

But opium, æther, camphor, alcohol, more quick, powerful, general, or diffusible stimulants, do they not first excite, stimulate, or (if you please) "increase the mobility of the nervous fluid;" but soon leaving the system in a situation directly opposite to their first impression, and to the same extent that the first impression or effect goes? Digitalis, cicuta, nitre, more local or fixed stimulants than the last, though perhaps not less powerful, or at least not less durable within the limits nature has

prescribed them, and indeed many of the stimulants and tonics of Dr. Cullen, do they not produce precisely the same effects; but within their more contracted sphere of action? Do they not effect an impression; in a word, stimulate the stomach, or (to use the language of Dr. Cullen) "increase the mobility of the fluid" in the nerves of the stomach? As well might we say, the impression from firing a cannon, the application of pepper to the tongue, or spirit of turpentine to a wound, were, and ought to be, called sedative operations, because they do not inflame the eye; as say, digitalis, cicuta, or nitre are sedatives, when we know the violent effects they have upon the stomach if taken in over doses. Can a stimulant be converted into a sedative, the reverse of itself, by lessening the dose? Here I might ask an explanation of the paradox, how a medicine\* introduced into, or applied to the body, can be a sedative? It must either produce an impression, or not, upon some one or other part; if it excites any part, it cannot be a sedative: if it does not, it must leave the body as it found it.

Dr. Cullen treats of sedatives under the heads of narcotics and refrigerents, and as they act more immediately on the nervous or sanguiferous systems. The former, says the Doctor, "diminish the sensibility and irritability of the system," or, in modern language, the excitability, "and thereby the

\* See note on this word in the fifth page.

" motions and powers of motion," or excitement in the system. This every body admits ; but we do not admit that it is done positively and directly, as he says ; but as it were negatively and indirectly by wasting the excitability, and (after a certain degree) by the excitement becoming less and less till it sinks below the healthy standard.

Contenting myself then with the simple idea of these, as well as all other medicines, being stimulants, and many of them of a violent kind too, I shall endeavour to account for the result of their exhibition.

I. It has been urged as a proof of the sedative operation of medicines, or that these kinds do not act by a stimulating virtue ; that there are no instances of any other medicines that stimulate, acting in such small quantities as narcotics : this objection may be answered by placing them at the head of stimulants. Of course then, they must act in the least, or very small quantities. Besides, this objection will equally hold good against their being sedatives ; for why should sedatives act in less quantities than stimulants ?

II. It is said, because these medicines, from frequent repetition, or in their successive application, require an increase of quantity to produce the same quantum of effect, they must therefore be sedative and not stimulant. Dr. Cullen appears to be of this opinion, when viewing it as a seeming inconsistency,

that the use of the most powerful tonics should ultimately occasion a total want of tone in the stomach, he throws out a conjecture, that they probably possess some narcotic or deleterious quality which injures the stomach.

If this be our criterion, we shall not find a stimulant in nature; not an operation which can be referred to that head: for there is no stimulant, internal or external, no impression that can be made, either on the organs of sense, or any other parts of our bodies, which, in the progress of its application, will not ultimately require an increase of quantity to produce the same sum of effect: or, if violent, will not induce a state of atony and indirect debility.

III. A great argument advanced in favour of this class of medicines, being sedatives, is derived from the soporific effects some of them possess, or tendency they have to induce the sleeping point. But how is sleep induced? Can it not be brought on by any other than a direct sedative operation? Or, rather is it not in common the effect of positive and direct stimulating operations?

Now I esteem it to be a just inference, that if we allow sleep is generally induced by directly stimulating operations, instead of sedative; and at the same time recollect, the most strenuous advocates for the sedative operation of medicines, still admit they have some stimulating effect. It is but just,

I say, to conclude—the soporific effects of this class of medicines, can be no proof of a direct sedative virtue in them; but rather proves them stimulants.

“Natural sleep,” says Dr. Rush, “is brought on by a diminution of the excitement and excitability, by the continual application of the stimuli which act upon the body, in its waking state”——“when the same number of stimuli act with the same force, and for the same time, upon the system, sleep will be induced at the same hour. But when they act with uncommon force, or for an unusual time, it is brought on at an earlier hour. Thus a long walk or ride, by persons accustomed to a sedentary life, unusual exercise of the understanding, the action of strong passions or emotions, and the continual application of unusual sounds,” (all these directly stimulating) “seldom fail of producing premature sleep. Artificial sleep may be induced at any time, by certain stimulating substances, as opium, &c.”†

Here it will be objected that a sedative operation, or an abstraction of usual stimuli, as light, sound, exercise, an erect posture, interesting thought, &c. must take place before sleep can possibly come on, which we contend sedatives effect or assist in bringing about in the body; for a person may bring on sleep, at any time, by darkness, silence, a recum-

† Lectures on Animal Life.

bent posture, temperate air, composure of mind, &c. It is to be sure a fact, that we find it necessary to remove many of the impressions acting in ordinary life upon our bodies, before sleep can take place: because the state of excitement they produce, whether it be observable by the senses or not, is nevertheless a state, on the one hand, above that of direct debility, and on the other, below that of indirect, wherein sleep comes on. Yet it is equally true these supposed direct sedatives can do away the effects of these impressions only in one way, so as to induce sleep, viz. by lessening, abstracting a part of, or fatiguing that principle on which they act, denominated stimulability, irritability, sensibility, or the excitability of Drs. Brown and Rush.

If the theoretical part of Dr. Brown's elements be admitted as authority, this opinion is strongly inculcated there: and Dr. Rush says, the excitability is wasted by the abstraction of stimuli, or, in other words, by a direct sedative operation, only in cases of a lingering or chronic nature. "Direct and indirect debility are upon a footing, when they are of a chronic nature, they both equally expend the excitability of the system."\* Now no one will contend, that those medicines, in the catalogue of sedatives, which are used to bring on sleep, have a slow or chronic operation on the system.

Instead then of the soporific effects of these medicines being a proof of their sedative nature, we

\* Lectures on animal life

must consider them as a proof of their exciting the animal body, or a particular system in that body, in a general and diffusible manner; and thus account for the waste of excitability, and that state of indirect debility which is followed by sleep. For these reasons—no medicines strictly sedative, or indeed of any class whatever, can possibly be so applied to the body, as to abstract the stimuli of ordinary life, whether the external, as light, sound, odours, air, heat; or the internal, as food, drink, chyle, blood, exercise of the mind, without irritation; they cannot neutralize them, or in any way prevent their application being made, or their presence existing: they can only lessen and prevent the impression taking effect, by diminishing the principle, as said before, on which they act, to produce their effect. These medicines cannot be sedatives, for then they must have a direct tendency to increase the excitability, and of course the sum of excitement, seeing they do not at the same time remove the stimuli; they can only be stimulants, or in any other way wear down the sensibility of the system to impressions.

Mr. Moore observes, “ It seems to me that narcotics occasion sleep, rather from counteracting the effects of the irritating causes above enumerated, than from a specific power of numbing the senses, and forcing them to sleep.” But they must counteract by creating a new action; if they do not, or if their effects were directly sedative;

they would bring on sleep at all times, under all circumstances; and the sooner and more perfect, the stronger they are, or greater the quantity. Instead of this, if you give a man, ready to drop asleep from fatigue and watching, a quantity of any soporific medicine, it will put off sleep for some time. They resemble precisely, in their operation, the impression and effect of mental and bodily exercise: let a person use these to such a degree as to induce fatigue, but not excessive, sound sleep will be the consequence; but extend them further, to excessive fatigue, they will prevent sleep. So, a moderate dose of some narcotics will cause that sleep, which double or triple the quantity would effectually prevent. Does the stimulus of mental and bodily exertion keep off sleep as long as the sensibility or excitability of the body is sufficient to support their effects? So does the impression of the soporific medicine, in every instance, without exception, according to the circumstances of the patient and medicine.

A question arises in this place; how can the stimulus of a narcotic produce that effect, which was just now observed to be prevented by the ordinary stimuli of life? I answer, this additional stimulus produces, in a short time, first the diminished state of excitability, and then of course excitement, which constitutes the sleeping point of indirect debility; a point that would have been brought on, in a greater space of time, by the ordinary stimuli of life. Or, if this will not be satisfactory, availing

myself of Dr. Rush's theory, wherein he divides the body into different systems, and contends for the independence and non-relation of these, to a considerable degree—of the translation of excitement and its determination to particular parts—of the translatable nature of Dr. Cullen's vis medicatrix; its being capable of a removal from some parts, and determination to others—I will say, in the language of the latter, when these supposed sedatives are given, the vis medicatrix is so much occupied in watching and expelling these dangerous enemies, that she neglects all other parts ; or, in the language of Dr. Rush, excitement is sooner or later diminished in the brain, eyes, ears, in short, all parts, whose state of action is more immediately concerned in keeping off sleep; and translated to parts, as the stomach, that do not sleep. There is a case in point we meet with every day; a hearty meal disposes to sleep; no one will say this is a sedative, or even that increased excitement does not exist at the time in the stomach; but rather, that indirect debility does exist, more especially in those parts, whose excitement more immediately keeps the person awake.

IV. A fourth reason given, for making these medicines sedatives, is derived from their power of relieving pain.

Mr. Moore, in his late concise but important essay upon the *materia medica*, while going on with his theory of sedatives, observes, “ the most re-

" markable effect of these medicines is, that of their  
 " assuaging, or entirely removing pain." After  
 confuting Dr. Cullen's theory and explanation of  
 their operation, he says, " it seems evident that  
 " narcotics act by exciting a strong affection in the  
 " brain, and not by rendering it torpid and insen-  
 " sible ; that the first impression is an excitement in  
 " the brain, is proven by the exhilaration which is  
 " generally seen upon swallowing the medicine, and  
 " by the increase of the action of the heart and  
 " blood vessels. Most narcotics occasion pain and  
 " inflammation when applied to any tender part, as  
 " the globe of the eye, or the surface of a wound.  
 " When an over-dose of narcotics produces torpor in  
 " the brain, or death, this is owing to the violent  
 " action they have upon it ; narcotics do not act by  
 " simply producing a torpid state of the brain ;  
 " they, on the contrary, excite it, but the excite-  
 " ment being different from that which is occasioned  
 " by the painful impression, counteracts its effect."\*

If narcotics relieve pain by a sedative virtue, how comes it to pass, that their local and direct application to the part pained, not only does not relieve pain, but will even increase it for a time, as when applied to wounds, &c.? And who would give a dose of a powerful narcotic, or sedative, if you please, in the height of gastritis; or in the most malignant and oppressed state of fever, where there is a want of action from an excess of stimulus? If the sedative operation of any medicine whatever was

simple and direct, that medicine, when used, would effect undoubtedly an entire quiet in a person in pain, and sooner, perhaps more effectually too, the nearer the pained part. Moreover, if there is any such medicine as a sedative, in our *materia medica*, or in nature, this medicine, exhibited in any state of pain and irritation however great, must not only counteract the disease, but likewise leave the system calm, unaffected, and composed ; in short, with every one of those pleasing and delightful feelings which always follow insensible and gradual depletion, as bloodletting, when judiciously prescribed : this is an occurrence that never takes place upon the exhibition of any known medicine, in these cases ; but like wave meeting wave, or wind opposed to wind, they give sufficient evidence of two stimulating operations contending for mastery in the system, even when they do relieve pain. I shall never forget my after-feelings in those few instances that I have had occasion to take an anodyne ; they cannot be better expressed, than by saying, I felt fatigued in every bone, muscle and nerve.

By allowing these medicines the simple property of stimulant, (and this, or some similar property they can only possess) I cannot help thinking their phœnomena and effects, when exhibited for the cure of pain, may be accounted for. To this end, let us enquire what the most probable theory of pain may be ? and how these remedies remove it ? If predisposing delibity (which is always attended, or soon

succeeded by increased sensibility to impressions) and in consequence of that excessive or morbid action in parts, from ordinary or extraordinary stimuli, cause pain; if wounds, bruises, burns, &c. induce pain; whether these are diseases of the whole system or only local, it is clear that these medicines by a stimulating operation, in some cases with, in others without previous depletion, might not only diminish but remove pain altogether. For by increasing the excitement in another part, they at least suspend it in the diseased part; by wasting a part of the excitability in a way less injurious to the system, they diminish it in the seat of the disease, or lessen its determination there, thus affording relief; by creating a disease or morbid excitement in a part less vital, or less weakened, they restore a better determination of excitability and excitement in the different divisions of the body; and remedy pain without forfeiting the character of stimulants; or at any rate, without affording positive proof of their virtue consisting in a direct sedative operation. Blisters applied to the extremities or near the diseased part, have relieved asthma, and violent pain: I would ask here, how the blisters act? not by a sedative operation; to be sure, if we confine our observation to the seat of the disease, we must say they are anodyne, they calm and compose; not by their inadequate quantity of evacuation alone; but by the additional aid of their stimulus in the seat.

of immediate application. How does mercury cure syphilis? How does fever stop the progress of chancre? How does a hearty meal cure a certain kind of head-ache? Not by abstracting the sensibility to impression, or the impression itself, from the body immediately and directly, (a sedative operation) though they may translate or give them a different direction. We cannot then, by any means, draw a satisfactory proof of the sedative operation of medicines, from the power they possess of relieving pain.

V. Another effect of some of these medicines, is to exhilarate and produce intoxication. One would think the bare mention of this effect sufficient, to shew the absurdity of calling narcotics sedatives, and remove every doubt about their operation. But if this be a sedative operation, how do you explain the fact, of great noise, mirth, a warm room, all expediting the inebriating quality of these supposed sedatives? How does exposure to cold, a far less questionable sedative operation, suspend their intoxicating virtue? I should think, on the one hand, those allowed stimulants, would rather do away than aid their effects; and on the other, cold would very much assist them.

VI. Equally impotent will all arguments be, taken from the successful application of these medicines, in cases of debility, spasm, and convulsion. "Narcotics," says Mr. Moore, "are given successfully, to diminish spasm and violent actions,

"likewise in cases of relaxation and debility, to increase the power of muscular contractions. I think these contradictions may be reconciled, and every effect of narcotics explained, by the principle formerly mentioned, that these substances *act* upon the brain, and are, in fact, stimulants."\*

The known good effects of allowed stimulant and tonic medicines in diseases of this description, can never be overbalanced by any supposed sedative virtue, in other medicines: and both the unity of truth, and the simplicity of nature, in all her operations, should make us decline referring to any new operation, the success that attends the use of narcotics, in these diseases of debility; at least, until this sedative virtue is well established.

As, in all probability, the removal of spasm, by these remedies, is effected upon the same principles, and in the same manner, as the diminishing of pain, we can make out nothing in favour of a sedative operation from this effect; especially, if we admit Dr. Rush's authority, when he says in his lectures on the practice, "the whole class of stimulant remedies, is indicated in some diseases of the spasmodic and convulsive kind."

Opium, a medicine generally allowed to have all the forementioned effects, and in fact, strongly marked with the features of narcotic sedatives, Dr. Barton makes this just observation upon; "It might be asked, why it is not used with success in inflammatory diseases, as well as venesection?

" But it never does good where venesection is necessary, according to Dr. Young : this is a golden rule, and cannot be too often impressed on the minds of young practitioners." — " The different degrees of diffusibility and durability of excitement that stimuli produce, accounts for the operation of opium."\* The rapid progress, a belief in the stimulating operation of opium is making, renders it unnecessary to dwell upon it : and as the first, in the most important division of sedative medicines, is thus converted into a stimulant, we have great encouragement to proceed in enquiring into the claim, the rest have to that virtue.

VII. Again it will be said, there are some medicines which have a direct sedative operation, for they diminish the action of the heart and arteries ; such as digitalis, saccharum, saturni, nitre, &c. But do these remedies, diminish the pulse in any other way than in point of frequency, or not ? If not, the effect may be by direct stimulus. Mr. Moore observes, " although they increase the force of the pulse, it is often found, that they decrease its frequency"— " the frequency of the pulse is often occasioned by its weakness ; these medicines by their stimulus increasing the force of the pulse, may lessen its frequency." This probably is one

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\* MS. Not; from Dr. Barton's Lecture on Opium.

reason why our predecessors styled them sedatives ; for their attention was principally directed to the frequency of the pulse. Admitting, however, that by lowering the pulse, is meant, a reduction in frequency and force ; is this a proof of these medicines being positively and directly sedative ? I answer no, it is not.

The slow, intermitting, depressed, imperceptible, and even paralytic states of the pulse, we are warranted in saying, may depend upon an excess of stimulus, instead of a direct sedative cause applied. For what other construction can you put upon the fact of some of those diseases which have heretofore been considered putrid, low, nervous (from indications of the pulse in common with other symptoms) being now placed first in the list of malignant and inflammatory diseases, and requiring the depleting plan of cure to its greatest extent ? Squills, we are informed, lower the pulse, and allum is said often to do it, this cannot be by a sedative virtue. Though some of these medicines may be indeed sedatives, with regard to that particular system, the sanguiferous ; do the blood vessels compose the whole body, or form a complete animal ? In deciding a question upon the operation of medicines, are we to throw out of the consideration every other part of the body, and attend to the blood vessels and their phenomena alone ? have we not frequent instances of disease affecting the nervous system while the blood vessels are apparently in health, of fever affecting the sanguife-

rous system, disorder the alimentary canal, in a great degree independent of each other? Equally as true, as natural, is the conclusion that medicines have the same partial operation, to a considerable degree. Important indications, perhaps the most important that can be drawn from any single division of the human body, may be taken from the blood vessels :\* but however greatly we may estimate them, and under the sanction of the highest authority, yet it is impossible to form correct ideas of the operation of medicines upon the *whole body*, by attending to their effects on any *one system*, though the most important, and most unerringly indicative of what is going forward in its own department. But we are giving far too much credit to the blood vessels : Dr. Cullen's and Dr. Hebenden's experience, give but little encouragement to expect such certain indications of what is going forward in the body, from the pulse alone.

Every one must know these medicines have strong and marked evidence of being stimulants. The digitalis is diuretic, much recommended in dropsy ; writers call it a virulent deleterious medicine, occasioning distressing sickness, violent vomiting, hypercatharsis, and disorder of the whole con-

\* Though the prevalence of this opinion may go to the neglect, and almost exclusion of the nervous system ; it does not appear more unreasonable to deprive a watch of its main spring, a clock of its weights, or ship of its sails and oars, than to exclude the nervous system from consideration, in physiology, pathology, or therapeutics.

stitution. Dr. Darwin, who places it in under his article *Sorbentia*, considering this medicine a violent stimulant says, " by its action the stomach is rendered torpid, with consequent sickness for days, owing to the great exhaustion of its sensorial power of irritation"—" and the action of the heart and arteries becomes feeble, from the deficient excitement of the sensorial power of association. The action of vomiting from the stronger emetics, as digitalis, is owing to deficiency of sensorial power, which is previously exhausted by the excess of its stimulus."\*

Why are we told squills are an excellent preparative for the exhibition of the digitalis; a stimulant to precede a sedative? experience teaches otherwise; a less stimulant may prepare the body for a greater; but illy suits to precede a medicine of so opposite a nature as a sedative. Dr. Beddoes removed the dangerous symptoms following the use of digitalis by large doses of opium. It is not conceivable that opium in large quantities can be proper in disease from direct sedative causes; for neither reason or experience, justify the exhibition of opium in large doses, where the patient is brought to the door of death by famine or depletion; and where sensibility and aptitude to impression and action are accumulated by sedative causes.

No one is a stranger to the diuretic and laxative effects of nitre, or those of *saccharum saturni*: when

\* *Zoonomia.*

taken through mistake, or intentionally, in too large quantities, or too often repeated, they bring on most violent affections of the primæ viæ, nausea, vomiting, purging; or constipation, colic, &c. Saccharum saturni sometimes produces salivation: and in the disease brought on by the introduction of lead into our bodies, it has been found necessary to recur to opium, alcohol, aromatics, in short a whole routine of remedies that undoubtedly have a stimulating virtue. It is presumable this very much favours the idea of its being a disease of indirect and not direct debility, and produced by the stimulus of the lead.

I conclude then, that under this view these medicines cannot be considered sedatives, with respect to the whole body: that they are disturbers of the present order and disposition of excitability and excitement; and that it is in every instance by *creating a new action* they produce their effects. Were their operation sedative, they would render the system more sensible to new impressions; whereas they have a tendency to lessen sensibility, or irritability for the time, however suddenly it may be accumulated afterwards.

VIII. From the operation of refrigerents in general (the second head of Dr. Cullen's sedatives) little evidence of a sedative virtue can be obtained. He defines them to be, "such medicines as diminish the temperature of the body when preterna-

“ turally increased\*.” His reasons for placing them under the head of sedatives, however they may impress conviction on some minds appear to me to have but little weight of proof: the words are, “ and as the heat of the body, whether from internal or external causes, is never increased beyond the ordinary decree, but with an increased action of the sanguiferous system; so the refrigerents as they diminish this increased action are justly put under the general title Sedantia.” We have formerly contended, that conclusive proof of a sedative virtue cannot be taken, from the fact of a medicine’s diminishing the action of the blood vessels alone, unless they composed the whole body; or, it was clearly ascertained, that no exciting and stimulating effect in any other division of the body was the consequence of its use. We find laxative, diuretic, stimulant, and even corrosive medicines included under this head of supposed sedatives, as Dr. Cullen himself acknowledges in the progress of his observations; some go so far as to place alkalis under this head; an arrangement apparently so contradictory and inconsistent, must at least have a tendency to make us suspect the sedative virtue of these medicines, or many of them.

Mr. Moore is of opinion, “ that the first action of refrigerents is produced by some impression upon the nerves of the stomach conveyed to the

" brain ; which impression occasions a diminution  
 " of the nervous influence sent to the heart and  
 " vessels, consequently the force of the circulation  
 " is lessened, and the heat of the body decreased."\*  
 Whatever we please to name this impression, or  
 whatever language we make choice of in describing  
 the particular principle and peculiar form of opera-  
 tion under which refrigerents act, the dispute will  
 be found to be about words only. It is the power  
 of sensation and motion, in a word the life of the  
 stomach, on which the refrigerent acts literally and  
 truly ; and it can be referred to no other operation,  
 or form of operation, than that of the most unques-  
 tionable stimulant, in the *materia medica*.

There are remedies of diseases which may be pro-  
 perly divided into those which primarily, and to a  
 great degree, insensibly diminish the stimuli to  
 which our bodies are exposed, as bleeding and the  
 gradual abstraction of heat ; and those which, in  
 the first instance, add to the quantity of stimuli  
 (as a dose of medicine) the effect of these must be  
 very different, each from the other.

Most medicines given, except diluents, and such  
 like, produce their primary effect by acting on the  
 nerves, not upon the contents of the *primæ viæ*,  
 vascular system, or any of the internal or external  
 stimuli that support life : this effect or excitement,  
 in the great and general view, must be the same  
 from whatever cause or remedy. But when the  
 medicine excites evidently, and a part that falls

under our observation, as opium the blood vessels, a purge the intestines, we say it stimulates.\* It is equally true, if not equally visible, that small quantities of neutral salts, diluted acids, or any other refrigerents, must act by irritation. The known effects of these in larger quantities, and a more concentrated state, prove it: the principle laid down before, that a medicine which does affect the body (but without producing a direct change in the various stimuli to which it is exposed) must affect, by exciting the nerves, proves it: the principle laid down, that the nervous power, or cause of sensation and motion, can only be lessened, in these cases, by impressions that have a resemblance in the main, and are called stimulating operations, proves it: and the diminished force of the circulation ought to be considered sufficient evidence (seeing no change or removal of stimuli takes place without irritation) of a new action existing somewhere: in short, we have no facts and conclusive evidence, in favour of a principle existing, or general form of operation, peculiar to narcotics and refrigerents, under which they act differently in the main, from the most unequivocal stimulant in medicine.

IX. Perhaps it might be said, diluents, attenuants, demulcents, &c. have a sedative operation.

\* Yet this purge may have an opposite but indirect effect upon another part. "They act, moreover, by creating an artificial weak part, and thus invite morbid excitement, from the blood vessels to the bowels."

Any matter applied to our bodies, or any causes, which have a stimulant operation, less than the ordinary stimuli of life; if so disposed of as to impede and prevent the action of these ordinary but greater stimuli, would be marked with such a result. Two grains of tartar emetic, in a large quantity of water, mucilage or oil, might have less effect upon the stomach, than when barely dissolved: but what does this prove? Exclude the ordinary stimuli of life, and while the body is suffering for want of them, apply these lesser stimuli, and mark the result: for instance, give a half famished man, a quantity of mucilage, oil, or even water, neither hot nor cold, and I am very much deceived, if he does not tell you, it affords a grateful impression, which can be called no other than a stimulating operation, though it be a small one.

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X. Whether we admit of vibrations in the nerves, of a refined fluid, or elastic vapour secreted in the brain, and conducted along tubes in the nerves—an elastic æther that pervades all nature, giving an electric virtue to glass, or magnetic to iron, and when particularly modified in the brain, becomes the principle of life—an electroid fluid produced by the friction of blood against the blood vessels—a particular modification of oxygen—or, a spirit of animation derived immediately from God—Still it is allowed—This unknown——is wasted or fatigued by the labours and afflictions of body and

mind, and recruited by rest and sleep—that the substances of the *materia medica* called stimulants, tonics, astringents, sedatives, or what, in common with all other sensible things, have an active impression, or effect upon *It*: which, though varying with various circumstances, and differing in degree, must at length be referred to one general principle, and one mode of operation.

I conclude then, with this corollary—If there be a sedative in nature, it is gradual and insensible depletion, (or the removal of something that stimulates,) such as blood letting, or the abstraction of heat, by the application of matter of a lower temperature; which is as literally, though not as effectual depletion, as blood letting.

F I N I S.





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